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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,826	12/13/2006	Marc W. Kirschner	H0498.70198US01	1753
86110 7590 10/02/2009 Harvard University & Medical School c/o Wolf, Greenfield & Sacks, P.C. 600 Atlantic Avenue Boston, MA 02210-2206				
EXAMINER				
GAKH, YELENA G				
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1797				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/550,826

Applicant(s)

KIRSCHNER ET AL.

Examiner

Yelena G. Gakh, Ph.D.

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF/ICE)
Paper No(s)/Mail Date 04/13/06, 06/21/07
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Preliminary amendment filed on 04/13/06 is acknowledged. Claims 1-33 are cancelled. Claims 34-49 are pending in the application.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 34-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 49 recite "exposing a sample containing a protein (a mixture of proteins) to a substrate", "allowing the protein to become immobilized with respect to the substrate", etc. It is not clear, which substrate is meant here. Is this a biological substrate? Is this a solid substrate? Is this a special substrate which is capable of chemical bonding to the protein?

From claim 38 it is not clear, which two different mass spectrometry techniques are meant here.

From claim 42 it is not apparent, as to which microarray is meant in the claim.

From claim 44 it is not clear which type of a self-assembled monolayer is meant in the claim.

Claim 48 recites the limitation "each entity", which lacks an antecedent basis, since no plurality of entities is recited in the parent claim.

The Applicants are respectfully referred to the following excerpt from MPEP:

"§2171 Two Separate Requirements for Claims Under 35 U.S.C. 112, Second Paragraph:

The second paragraph of 35 U.S.C. 112 is directed to requirements for the claims: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

There are two separate requirements set forth in this paragraph:

- (A) the claims must set forth the subject matter that applicants regard as their invention; and

- (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

The first requirement is a subjective one because it is dependent on what the applicants for a patent regard as their invention. The second requirement is an objective one because it is not dependent on the views of applicant or any particular individual, but is evaluated in the context of whether the claim is definite - i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art.

Although an essential purpose of the examination process is to determine whether or not the claims define an invention that is both novel and nonobvious over the prior art, another essential purpose of patent examination is to determine whether or not the claims are precise, clear, correct, and unambiguous. The uncertainties of claim scope should be removed, as much as possible, during the examination process.

The inquiry during examination is patentability of the invention as applicant regards it. If the claims do not particularly point out and distinctly claim that which applicants regard as their invention, the appropriate action by the examiner is to reject the claims under 35 U.S.C. 112, second paragraph. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). If a rejection is based on 35 U.S.C. 112, second paragraph, the examiner should further explain whether the rejection is based on indefiniteness or on the failure to claim what applicants regard as their invention. *Ex parte Ionescu*, 222 USPQ 537, 539 Bd. App. 1984)"

Furthermore:

"§2172 Subject Matter Which Applicants Regard as Their Invention:

If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int 'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)."

In the instant case "the language of the claims is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement", which makes the rejection under 35 U.S.C. 112, second paragraph appropriate.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. **Claims 34 and 36-38** are rejected under 35 U.S.C. 102(b) as being anticipated by Nelson (Mass Spec. Rev., 1997).

Regarding *claims 34 and 36-38* Nelson discloses a method of mass spectrometry, comprising:

- exposing a sample containing a protein to a substrate;
- allowing the protein to become immobilized with respect to the substrate;
- exposing the protein immobilized with respect to the substrate to mass spectral ionization conditions to generate ionized fragments;
- determining, via analysis of the identity of the ionized fragments, the identity of the protein,

wherein MALDI or MALDI-TOF mass spectrometry is used and wherein at least a portion of a primary sequence of the protein is determined. (See page 355, right column and page 356, left column).

6. **Claims 34, 36, 38, 44, 46-48** are rejected under 35 U.S.C. 102(b) as being anticipated by Parker et al. (Mol. Biol., January 2002) (Parker).

Regarding *claims 34, 36, 38, 44 and 46-48* Parker discloses the following:

"Proteolytic digestion of proteins bound to immobilized antibodies, combined with matrix assisted laser desorption (MALDI) mass spectrometric identification of the affinity-bound peptides, can be a powerful technique for epitope determination. Binding of the protein to the antibody is done while the protein is in its native, folded state. A purified protein is not required for this procedure, because only proteins containing the antigenic determinant will bind to the antibody in the initial step. The method makes use of the resistance of the antibody to enzymatic

digestion. Enzymatic cleavage products of the antigenic protein not containing the epitope are washed off the beads, leaving the epitope-containing fragments affinity bound to the immobilized antibody. Dissociation of the antigen-antibody complex prior to mass spectrometric analysis is unnecessary because the affinity-bound peptides are released by the MALDI matrix crystallization process, although the antibody remains covalently attached to the sepharose beads." (Abstract).

7. **Claims 34-37 and 40-49** are rejected under 35 U.S.C. 102(a) as being anticipated by Duffy (US 2002/0028463).

Duffy discloses forming various substrates for detecting interactions between biomolecules, including proteins, by e.g. immobilizing proteins (par. [0027]) (*Claims 34, 35 and 40*), in some embodiments in arrays (par. [0028]) (*Claims 42 and 43*), including cell lysates (par. [0030]), wherein substrates can comprise self-associated monolayers on gold (par. [0077]) (*Claims 44, 45*). In Paragraph [0113] Duffy indicates that "[m]odifications or binding of biomolecules in solution or immobilized on an array may be detected using detection techniques known in the art", which include MALDI (*Claim 36*) and MALDI-TOF (*Claim 37*). Examples disclosed in paragraphs [0132] and [0133] disclose washing the substrate after immobilization of the proteins, which inherently washes away non-bound proteins (*Claims 35 and 49*). Specific binding is disclosed in par. [0026] (*Claim 46*). Binding to antibodies is disclosed in par. [0038] (*Claims 47, 48*).

8. **Claims 34-37, 39-40, 42-44, 46 and 49** are rejected under 35 U.S.C. 102(a) as being anticipated by Su et al. Angew. Chem. Int. Ed., December 2002, IDS (Su).

Su teaches immobilizing ligands to isolate active proteins from the background in a complex sample, which simplifies the analysis of MS spectra by combining MALDI and MALDI-TOF with self-assembled monolayers (SAMs) that are engineered to give specific interaction with biomolecules (page 4717). The unbound proteins are washed away. Su specifically indicates that availability of protein arrays makes this technique immediately applicable (page 4718).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. **Claims 38 and 39** are rejected under 35 U.S.C. 103(a) as being unpatentable over Duffy.

While Duffy does not specifically teach determining at least a portion of a primary sequence of the protein or applying tandem mass spectrometry, these techniques are conventional in the prior art, and therefore it would have been obvious for a person of ordinary skill in the art to expand Duffy's analysis of proteins immobilized on the substrates using tandem MALDI-TOF/TOF for determining at least a portion of primary sequence of the protein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Y. Kim can be reached on (571) 272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

9/29/2009